1.0 PURPOSE

The Division of AIDS (DAIDS), National Institute of Allergy and Infectious Diseases (NIAID) has established specific requirements for laboratories processing and testing biologic samples from participants enrolled in clinical trials sponsored and/or funded by DAIDS. These requirements relate to general laboratory operations, quality assurance and control procedures, management of specimens and management of laboratory data. The purpose of this policy is to safeguard participants enrolled in clinical trials and to ensure the reliability and validity of all laboratory measurements taken to determine eligibility, identify and manage adverse events, and assess outcomes during the course of the clinical trial.

2.0 SCOPE

This policy applies to all laboratory procedures in support of a therapeutic, vaccine, or prevention clinical trial funded and/or sponsored by DAIDS.

3.0 BACKGROUND

This policy identifies requirements regarding laboratory operations in order to ensure compliance of US laboratories with the federal Clinical Laboratory Improvement Amendments (CLIA) rules (42 CFR Part 493), and the Code of Federal Regulation for Good Laboratory Practices (21 CFR Part 58). The purpose of these regulations is to promote good laboratory practices and to assure reliable laboratory results and documentation/records. Regulations under these guidelines define requirements for personnel, procedures, and policies. DAIDS strives to achieve an equivalent level of quality in the operations of its non-US laboratories that support DAIDS international trials.

4.0 DEFINITIONS

See DAIDS glossary.

5.0 RESPONSIBILITIES

This policy, and the associated specific requirements for US and non-US laboratories has been created by DAIDS staff whose responsibility is to oversee the laboratory component of DAIDS clinical trials. DAIDS staff will be responsible for updating this standard in response to changes in Federal regulations and based on continued experience in the conduct of clinical trials. DAIDS staff will be responsive to queries by investigators who need assistance with understanding this policy and with implementing the specific requirements for US and non-US laboratories.

The Principal Investigator is responsible for ensuring that laboratories processing and testing biologic samples from participants enrolled in clinical trials adhere to the laboratory requirements identified in this policy.

6.0 POLICY

DAIDS has established and maintains specific requirements for laboratory performance in six areas:

I. Diagnosis, Safety Tests, CD4 and Virological Tests

Tests that are used for diagnosis of infection, determining eligibility, endpoints, monitoring the safety of the intervention and making patient management decisions must be performed in laboratories that conduct operations in a Good Clinical Laboratory Practices (GCLP) manner and tests must be quality assured by external proficiency testing surveys. When not available, external quality assurance measures should be devised. US laboratories must be CLIA-certified and non-US laboratories are encouraged to become accredited by CLIA or an equivalent organization.

II. Research Use Only (RUO) Tests (research tests not yet validated and approved by an ICH regulatory body such as the FDA)

Research Use Only endpoint tests should be performed in laboratories that conduct operations in a GCLP manner. External proficiency testing (PT) should be applied. It is recommended that GCLP and external PT be applied also to non-endpoint RUOs.

III. Study Specimen Management

Procedures for the management of trial specimens must be documented and followed to ensure the integrity of specimens and their timely testing. Procedures should address specimen acquisition, receipt, processing, testing, storage, shipping according to regulations (e.g. International Air Transport Association (IATA)) and under conditions that preserve specimen integrity (e.g. maintaining the cold chain), and tracking.

IV. Study Laboratory Data Management

Procedures for the management of laboratory data must be documented and followed to ensure data integrity and timely reporting of results and should include appropriate procedures for data QA and corrective actions. Procedures should address data acquisition, recording/entry, data modification, signatures, export, archiving and security, as well as integration of the laboratory data with the main study database. Computerized laboratory systems should be validated, taking into account the elements of 21 CFR part 11 compliance.

V. Laboratory Quality Assurance

Laboratories that are not accredited by CLIA or equivalent organization must have a laboratory quality assurance plan to regularly review all components of laboratory activities, including intervention and corrective action plan, and plans for backup testing facilities.

VI. Laboratory Audits Provided by DAIDS

DAIDS and/or its contractors will conduct laboratory-specific audit visits to determine laboratory readiness to participate in trials, and, as indicated, during the conduct of a trial.

These laboratory requirements are reviewed periodically and updated as necessary to maintain currency with accepted practices and technological innovation. For the convenience of current and potential investigators and collaborating laboratories, separate documents are available for US based laboratories (Appendix 1) and non-US laboratories (Appendix 2). Differences in these documents pertain largely to laboratory accreditation bodies and procedures within and outside of the United States.

Comprehensive Laboratory Plan: Applications in response to PAR-05-113 'NIAID Clinical Trial Implementation (U01) Cooperative Agreement' must include a Comprehensive Laboratory Plan in the Appendix that identifies all proposed laboratories and plans to ensure they meet DAIDS requirements. The required content and suggested formats for components of the Comprehensive Laboratory Plan are detailed in the above referenced documents.

7.0 REFERENCES

U.S. Code of Federal Regulations 21 CFR Part 11
http://www.fda.gov/ora/compliance_ref/part11/

U.S. Code of Federal Regulations 21 CFR Part 58
http://www.access.gpo.gov/nara/cfr/waisidx_01/21cfr58_01.html

U.S. Code of Federal Regulations 42 CFR Part 493
http://www.phppo.cdc.gov/clia/pdf/CMS-2226-F.pdf

CLIA Program – Clinical Laboratory Improvement Amendments
http://www.cms.hhs.gov/clia/

DHHS/CDC Presentation
http://www.phppo.cdc.gov/dls/ila/cd/botswana/Presentations/QS%20-%20Overview.ppt

MMWR 1997; 46 No. RR-2 Dual-platform technology
http://www.cdc.gov/mmwr/preview/mmwrhtml/00045580.htm

MMWR 2003; 52(RR-2) Single-platform technology
http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5202a1.htm

International Air Transport Association (IATA) Shipping Regulations
http://www.iata.org/ps/publications/9065.htm

8.0 INQUIRIES

Questions and comments regarding this policy may be directed to the OPCRO Policy Group at:

NIAIDOPCROPOLICYGROUP@mail.nih.gov

9.0 AVAILABILITY

This policy is available electronically at the following URL:
http://www3.niaid.nih.gov/research/resources/DAIDSClinRsrch/Default.htm

The signed original is maintained in the OPCRO policy office.

10.0 CHANGE SUMMARY

Version #	Date	Replaces	Date of Revision	Rationale for Revision/Retirement
1.0	14 JUL 06	N/A	N/A	N/A

11.0 APPENDICES

Appendix 1 - DAIDS Requirements for US Laboratories

Appendix 2 - DAIDS Requirements for non-US Laboratories

12.0 APPROVAL

	Signature	Program/Branch	Date
Authorized By:	Richard Hafner, MD Director	Office for Policy in Clinical Research Operations	July 14, 2006